AFFECT OF MUTATIONS IN THE PRION PROTEIN ON PROCESSING IN TRANSFECTED HUMAN CELL LINES. R.B. Petersen, S.L. Richardson, C.B. Urig, P. Parchi, S.I.A. Zaidi, Neenah Singh, S. G. Chen, and P. Gambetti. Institute of Pathology, Case Western Reserve University, 2085 Adelbert Road, Cleveland, Ohio 44106

The prion protein, PrP, is associated with a number of neurodegenerative diseases which can occur sporadically, by transmission, or through inheritance of a mutated gene. Despite the various means of acquisition these diseases are unified by the presence of protease resistant PrP in the brain of affected individuals. The protease resistance is correlated with an altered conformation of the PrP; as is the case in Alzheimer disease the change seems to involve a transition of alpha helical regions to beta pleated sheets. The mechanism by which this transition occurs and is subsequently propagated is unknown. A wide variety of pathogenic mutations in PrP have been described which cause GSS, familial CJD, and FFI. We created cell lines expressing either normal or mutant PrP to study the effect of the mutations on the metabolism of PrP. We used a homologous system, the human PrP coding sequence and the human neuroblastoma cell line M17, to simplify analysis. Our findings show that the mutations can result in altered metabolism of the prion protein and that the different mutations have different effects. This work was supported by NIH grant AG-08992 and AG-08155.